ORIGINAL ARTICLE

Laparoscopic myomectomy for infertile patients with intramural fibroids: A retrospective study at a tertiary endoscopic centre

R J Lourens, MB ChB
T I Siebert, MMed (O&G), PhD
T F Kruger, MMed (O&G), MD
J P van der Merwe, MMed (O&G)
Department of Obstetrics and Gynaecology, Stellenbosch University, Tygerberg, W Cape

Background. The safety of laparoscopic myomectomy has been questioned, especially in the case of fibroids.

Objectives. To assess the safety of laparoscopic myomectomy for intramural fibroids and study the subsequent effect on fertility.

Methods and settings. A retrospective study of a tertiary endoscopic centre specialising in laparoscopic myomectomy.

Results. Eighty-seven patients were studied, and there were no major complications. The conversion rate from laparoscopy to laparotomy was 3.4% (3/87), in all cases due to multiple fibroids. There was 1 case of uterine perforation during hysteroscopy. The overall pregnancy rate was 29/64 (45.3%), with a spontaneous pregnancy rate of 18/29 (62.0%).

Conclusions. Laparoscopic myomectomy can be regarded as a safe alternative to abdominal myomectomy in the hands of the experienced surgeon, resulting in good subsequent pregnancy rates.

Uterine fibroids are the most common solid pelvic tumours in females. Fibroids have a reported incidence ranging from 30% to 70% in women of reproductive age and increasing with age.[1] A large percentage of fibroids are undiagnosed, since many are asymptomatic. The real incidence of fibroids is therefore unknown. The peak incidence is between 35 and 49 years.[1] Black women are 3 - 9 times more likely to suffer from uterine fibroids compared with European ethnic groups.[2] Risk factors for fibroids include nulliparity, obesity, black ethnic group, family history, polycystic ovarian syndrome, diabetes and hypertension.[3,4] Patients with uterine fibroids usually present with excessive or irregular vaginal bleeding, infertility or pain.

There is no clear evidence on whether it is safer to remove intramural fibroids by laparoscopy or by laparotomy. One of the biggest case series on the safety of laparoscopic myomectomy studied 265 women who underwent laparoscopic myomectomy. In that series subserosal and intramural fibroids were removed, with a conversion rate of 11.3% from laparoscopy to laparotomy.[5] A meta-analysis of laparoscopic versus open myomectomy overall found fewer complications in the laparoscopic group. No clear distinction was made between subserosal and intramural fibroids.[6] With the new and rapid development in laparoscopic surgery equipment and skills, the question is asked why so many myomectomies are still done as an open procedure. The most likely answer is a lack in surgical skill.

The relationship between infertility and uterine fibroids is well known. However, the effect of location and size of fibroids on fertility is not clear. It has been proved that the removal of submucosal fibroids improves fertility, but removal of subserosal fibroids has no impact on fertility.[7,8] Great uncertainties exist about the effect of intramural fibroids on fertility.

A possible explanation for the lack of evidence of the effect of intramural fibroids on fertility may be the large variety of methods for assessing the intra-uterine cavity reported in the literature.[8] The gold standard used to be the hysterosalpingogram (HSG), with or without an

ultrasound scan.[9] This has been replaced by hysteroscopy. Benecke *et al*. have suggested that intramural fibroids should be removed if they are close to the endometrium (<1 cm) and larger than 20 mm.[10]

Few studies have evaluated the safety of and fertility rates associated with laparoscopic myomectomy for the *treatment of intramural fibroids alone*.

Our aim was to evaluate the safety of laparoscopic myomectomy of intramural fibroids and the impact on subsequent fertility.

Material and methods

Setting

A retrospective and observational audit was done and data were collected from 1 January 2006 until 30 April 2009. The setting was a tertiary endoscopic centre at Vincent Pallotti Hospital, Cape Town (Centre for Reproductive Medicine and a referral centre for endoscopic procedures). The first arm of the study assessed the safety of laparoscopic myomectomy, and the second arm the fertility of patients who had had laparoscopic myomectomy. A detailed retrospective review of 87 patients' case records was done, which included telephonic interviews. Of the 87 cases reviewed, infertility was the main complaint in 71 (81.6%). Menorrhagia was the main complaint in the remaining 16 cases (18.4%). All 87 cases were included in evaluation of the safety of laparoscopic myomectomy. However, when subsequent fertility was evaluated 7 of the 71 cases were excluded because the patients did not continue to pursue a pregnancy after the operation.

Analysis of data

MS Excel was used to capture the data and STATISTICA version 10 (StatSoft Inc. (2011) STATISTICA (data analysis software system), www.statsoft.com) to analyse the data.

The primary objective of the study was to determine the complication rate. This was analysed by means of absolute and relative frequencies, together with appropriate 95% confidence intervals (CIs) as an estimate of the population proportion.

The relationships between continuous response variables and nominal input variables were analysed using appropriate analysis of variance (ANOVA). When ordinal response variables were compared versus a nominal input variable, non-parametric ANOVA methods were used. For completely randomised designs the Mann-Whitney test or the Kruskal-Wallis test were used, and for repeated measures the Wilcoxon or Friedman tests were used. The relationship between two nominal variables was investigated with contingency tables and likelihood ratio chi-square tests.

A *p*-value of <0.05 represents statistical significance in hypothesis testing, and 95% CIs were used to describe the estimation of unknown parameters.

The pre-operative work-up included a thorough history, examination, confirmation of ovulation in the fertility group, and a vaginal ultrasound scan. In theatre all patients had a hysteroscopy before the laparoscopy.

Equipment

Standard laparoscopic equipment was used in a laparoscopic theatre layout with high-definition screens. A 3D-chip camera was used. For the routine hysteroscopies a 3 mm Betocchi hysteroscope with normal saline to distend the uterine cavity was used.

Procedure

Routine hysteroscopy was done using the Betocchi hysteroscope (Storz®) to evaluate the uterine cavity before laparoscopy.

Laparoscopy with 4-port access was performed. The area around the fibroid was infiltrated with ornipressin (a vasopressin) using a 20 IU in 30 ml normal saline solution to minimise blood loss. Monopolar cautery was used for the incision. After the myomectomy the uterus was closed in separate layers. The muscle was closed in 1 - 2 layers with Vicryl 3/0 and the serosa was closed with Prolene 3/0. This slowly absorbed monofilament suture was used to minimise the risk of adhesions.

Surgeons' experience

Three experienced laparoscopic surgeons performed the procedures. The management of severe endometriosis makes up the bulk of their work.

Inclusion criteria

The inclusion criterion was either menorrhagia or infertility thought to be caused by intramural fibroids. The criteria for surgery were the following:

- the fibroids had to be intramural
- 20 - 60 mm in size
- less than 10 mm from the endometrial cavity or
- distort the cavity or
- multiple intramural fibroids.

This study was ethically approved by the Human Research Ethical Committee of Stellenbosch University (Institutional Review Board Number: IRB0005239).

Results

A total of 87 patients were studied, 71 of whom were treated for infertility and 16 for menorrhagia. The main aim of the study was to study the safety profile of laparoscopic myomectomy. The outcome measures were blood vessel injury, bowel injury, postoperative infection and conversion to laparotomy. The second aim was to

study fertility rates after laparoscopic myomectomy. The mode of delivery was also noted. The average age of the subjects was 36 years.

Safety

All 87 patients were included to evaluate the safety of laparoscopic myomectomy. There were no major blood vessel injuries, postoperative haemorrhage, bowel injuries or postoperative infections. There was 1 case (1.1%) of uterine perforation during hysteroscopy.

In total there were 3 conversions from laparoscopic myomectomy to laparotomy (3.4%). In all 3 cases the procedure became technically difficult and it was unacceptably hazardous to proceed laparoscopically because of the large and multiple fibroids that were encountered. Of these 3 patients, 2 (2.3% of the total) were from the menorrhagia group and 1 (1.1%) was being treated for infertility. On average two fibroids were seen pre-operatively. The average size of the fibroids in the laparoconversion group was 47.7 mm, which was bigger than the average size of 31.7 mm in the remaining patients in whom there were no complications. There was a trend towards a higher risk of conversion to laparotomy with larger fibroid size, although this was not statistically significant (p=0.09) (Table I).

None of the patients complained of prolonged postoperative pain (more than 6 weeks).

Fertility outcome

Seventy-one patients were eligible to evaluate fertility as a secondary outcome. Of these, 7 (9.9%) were excluded owing to lack of information, leaving 64 (90.1% of the 71) who could be evaluated to determine fertility outcome.

The following fertility outcomes were observed. The overall pregnancy rate after myomectomy was 29/64 (45.3%). Of the 29/64 (45.3%) patients who fell pregnant, 18/29 (62.1%) conceived naturally. The remaining 11/29 (37.9%) conceived with assisted reproduction (Table II). Of the assisted reproduction group, 1/11 (9.1%) had ovulation induction with clomiphene citrate, 2/11(18.2%) had intracytoplasmic sperm injection (ICSI), 4/11 (36.4%) had *in vitro* fertilisation (IVF) and 4/11 (36.4%) had artificial insemination (AI). Of the non-pregnant group, 9/35 (25.7%) attempted assisted reproduction. In all cases conception was achieved within 12 months postoperatively.

The average size of the fibroids in the pregnant group was 30.9 mm (SD 15.47 mm) (95% CI 25.17 - 36.63 mm), and in the non-pregnant group it was 28.48 mm (SD 16.41 mm) (95% CI 22.88 - 34.08 mm). In the pregnant group 85.7% of fibroids were against the uterine cavity, compared with 87.9% in the non-pregnant group. This was not statistically significant (p=0.08). There was cavity distortion in 14.3% of the pregnant group and 30.3% of the non-pregnant group. This was also not statistically significant (p=0.138) (Table II).

In 8/87 cases (9.2%) submucosal fibroids were diagnosed on routine hysteroscopy. These fibroids were sonographically misdiagnosed as intramural fibroids distorting the cavity. This result emphasises the point that hysteroscopy should be done at the time of laparoscopy.

In the group (29/64, 45.3%) who fell pregnant, 22/27 of patients (81.5%) had live births and 5/27 (18.5%) spontaneous miscarriages. We were unable to contact 2 patients (2/29, 6.9%) to establish whether the pregnancy had resulted in a live birth or a miscarriage. Of the live births 5/22 (22.7%) were preterm. The mode of delivery in all patients but one was caesarean section. There were no reported uterine ruptures.

Discussion

Safety

The optimal route of removal of *intramural* fibroids has long been a topic of discussion. However, there is still much dispute as to which is the most appropriate and safest route of removal. It is also still inconclusive whether intramural fibroids do in fact cause infertility.[8] One of the reasons for the lack of evidence is the absence of reports on the evaluation of the uterine cavity before removal.[8] Another reason could be the lack of randomised controlled trials, but it would be difficult to justify such a study ethically. In a large systematic review three factors were of concern regarding the removal of intramural fibroids: these are intra- and postoperative complications, postoperative adhesions, and the future risk of uterine rupture leading to an increase in the number of caesarean sections.[8]

Table I. **Safety of laparoscopic myomectomy**

Description	Fertility group (*N* (%))	Menorrhagia group (*N* (%))	Total
Patients studied	71 (81.6)	16 (18.4)	87
Conversions to laparotomy	1	2	3/87 (3.4)
Uterine perforation	1	0	1/87 (1.1)
Intra-operative haemorrhage	0 (0)	0 (0)	0 (0)
Postoperative haemorrhage	0 (0)	0 (0)	0 (0)
Bowel injuries	0 (0)	0 (0)	0 (0)
Postoperative infections	0 (0)	0 (0)	0 (0)

Table II. Fertility outcomes

Description	Fertility group (*N* (%))		Menorrhagia group (*N* (%))
No. of patients	71		16
Patients excluded	7/71 (9.9)		16/16 (100)
	Pregnant group	**Non-pregnant group**	
Total No. pregnant	29/64 (45.3)	35/64 (54.7)	
Conceived spontaneously	18/29 (62.1)	N/A	
Assisted reproduction	11/29 (37.9)	6/19 (31.6)	
Cavity distortion	4 (14.3)	10 (30.3)	
Fibroids close to cavity	24 (85.7)	29 (87.9)	
Live births	22/27 (81.5)	N/A	
Preterm births	5/22 (22.7)	N/A	
Spontaneous miscarriages	5/27 (18.5)	N/A	

In this study there were no intra- or postoperative complications other than one perforation of the uterus during hysteroscopy and conversion to laparotomy in 3 cases. It also seems that when considering a laparoscopic myomectomy the size, location and the number of fibroids present have to be taken into account.[11,12] It is our opinion that conversion to laparotomy cannot be seen as a complication, but rather an intervention to prevent further complications. In 2001 Dubuisson *et al*. reported an 11.3% conversion rate to an open procedure.[5] They found the main risk factors to be size (>50 mm), anterior location, intramural fibroids and the use of gonadotrophin-releasing hormone (GnRH) agonists pre-operatively. Patients with subserosal and intramural fibroids were included. Fibroids larger than 60 mm in diameter should preferably be removed via a laparotomy, as they tend to increase the risk of conversion from laparoscopy to laparotomy. In this study it appeared that the likelihood of conversion to laparotomy increased with larger fibroids, especially if they were larger than 47 mm in diameter.

There were no uterine ruptures during any of the pregnancies. All the patients but one were delivered by caesarean section, with no major complications reported. In a prospective study of 111 women after laparoscopic myomectomy, 79% delivered vaginally with no reported cases of uterine rupture.[13] In a retrospective study of 159 women, 74% delivered by caesarean section and 25% vaginally, and no uterine ruptures were reported.[14] However, it was not stated what the mode of delivery was in those patients in whom the cavity was opened. One should be cautious in opting for vaginal birth in cases where the cavity has been breached. Each case must be individually evaluated and counselled on the risks of attempted vaginal birth versus elective repeat caesarean section, for no site and size of uterine incision are the same. Currently no clear guidelines exist regarding the choice of mode of delivery after myomectomy.

A recent meta-analysis on laparoscopic versus open myomectomy showed reduced blood loss, postoperative pain and overall complications to be associated with laparoscopic myomectomy.[6] However, operating time was increased in the laparoscopic group. Patients in the laparoscopic group had a higher probability of conceiving, but no statistical difference in pregnancy rates could be reached. In this review of 7 studies there were only 6 cases reported in which a conversion to laparotomy was performed. The reasons quoted for the conversions were haemostasis, suturing time, size and number of fibroids and anaesthetic problems. However, the report made *no distinction between subserosal and intramural fibroids*. Comments about implantation rates are therefore difficult to interpret.

Fertility

The debate about whether non-distorting intramural fibroids cause infertility was raised by Pritts in a 2001 review.[15] It was found that only submucous fibroids and fibroids with an intracavitary component were associated with lower implantation, pregnancy and delivery rates. Subserosal fibroids have no impact on fertility. At that time there was no evidence that intramural fibroids with no intracavitary component caused infertility. In 2001 Hart *et al*. found that in patients undergoing assisted reproduction the presence of intramural fibroids halves the chance of an ongoing pregnancy.[16] In 2005 Benecke *et al*. emphasised the negative impact of intramural fibroids on fertility.[10] This was especially evident in implantation, pregnancy and live birth rates. They advised that intramural fibroids close to the cavity (<1 cm), those greater than 2 cm in size and multiple intramural myomas should be removed surgically to improve fertility. This relationship between intramural fibroids without intracavitary involvement was confirmed by Pritts *et al*.'s 2009 review.[8] However, it is not certain whether removal of these fibroids affects fertility. Compared with controls with fibroids *in situ*, removal of intramural fibroids resulted in no statistical significance in pregnancy rates.

One of the reasons for the reported result could be poor evaluation of the uterine cavity at the time of surgery.[8]

Evaluation of the intra-uterine cavity before removal of fibroids is essential. The gold standard for evaluating the cavity was the hysterosalpingogram (HSG).[17] However, an HSG has a sensitivity of 50% and a positive predictive value of 25% in picking up intra-uterine abnormalities, whereas hysteroscopy has near 100% sensitivity. Studies have shown that a sonohysterogram is more accurate than an HSG in diagnosing intra-uterine abnormalities. None of the above is as accurate as hysteroscopy, which is now considered to be the gold standard for evaluating the uterine cavity.[17,18] Hysteroscopy is therefore the method of choice, and should be done in every case on the day of laparoscopic surgery when intramural fibroids are suspected to be the cause of infertility. In our study 9.2% of patients were found to have submucous fibroids at hysteroscopy, as well as intramural fibroids which it is important to remove at the time of the planned laparoscopic surgery.

From these audit data we suggest that a woman whose infertility is probably attributable to intramural fibroids (as diagnosed by the strict inclusion criteria) will have a 40 - 60% chance of conceiving spontaneously within 6 - 12 months once the fibroids have been removed laparoscopically. This compares quite favourably with international data.[19]

Conclusion

Laparoscopic myomectomy can probably be regarded as a safe alternative to laparotomy. We are also of the opinion that if an intramural fibroid is suspected to be causing infertility, and it fits within the set criteria, its removal is likely to improve fertility. This is extremely important for developing countries where assisted reproductive techniques are not subsidised by government, and correct surgical practice can have a huge impact on the fertility prognosis of our patients. These results also emphasise the importance of proper endoscopic training to increase the safety of the procedure.

1. Okolo S. Incidence, aetiology and epidemiology of uterine fibroids. Best Pract Res Clin Obstet Gynaecol 2008;22(4):571-588.
2. Buttram VC Jr. Uterine leiomyomata – aetiology, symptomatology and management. Prog Clin Biol Res 1986;225:275-296.
3. Vollenhoven B. The epidemiology of uterine leiomyomas. Baillière's Clin Obstet Gynaecol 1998;12(2):169-176.
4. Flake GP, Andersen J, Dixon D. Etiology and pathogenesis of uterine leiomyomas: a review. Environ Health Perspect 2003;111(8):1037-1054.
5. Dubuisson JB, Fauconnier A, Fourchotte V, Babaki-Fard K, Coste J, Chapron C. Laparoscopic myomectomy: predicting the risk of conversion to an open procedure. Hum Reprod 2001;16(8):1726-1731.
6. Chu J, Yan H, Xia-Chan C, et al. Laparoscopic versus open myomectomy – a meta-analysis of randomised controlled trials. Eur J Obstet Gynecol Reprod Biol 2009;145(1):14-21.
7. Eldar-Geva T, Meagher S, Healy DL, Mac-Lachlan V, Breheny S, Wood C. Effect of intramural, subserosal and submucosal uterine fibroids on the outcome of assisted reproductive technology treatment. Fertil Steril 1998;70:687-692.
8. Pritts EA, Parker WH, Olive DL. Fibroids and infertility: an updated systematic review of the evidence. Fertil Steril 2009;91(4):1215-1223.
9. Soares SR, Barbosa dos Reis MM, Camargos AF. Diagnostic accuracy of sonohysterography, transvaginal sonography, and hysterosalpingography in patients with intrauterine cavity diseases. Fertil Steril 2000;73(2):406-411.
10. Benecke C, Kruger TF, Siebert TI, Van Der Merwe JP, Steyn DW. Effect of fibroids on fertility in patients undergoing assisted reproduction. Gynecol Obstet Invest 2005;59:225-230.
11. Sinha R, Hegde A, Mahajan C, et al. Laparoscopic myomectomy: do size, number, and location of the myomas form limiting factors for laparoscopic myomectomy? J Minim Invasive Gynecol 2008;15(3):292-300.
12. Marret H, Chevillot M, Giraudeau B, et al. Factors influencing laparoconversions during the learning curve of laparoscopic myomectomy. Acta Obstet Gynecol Scand 2006;85(3):324-329.
13. Kumakiri J, Takeuchi H, Itoh S, et al. Prospective evaluation for the feasibility and safety of vaginal birth after laparoscopic myomecmtomy. J Minim Invasive Gynecol 2008;15(4):420-424.
14. Seracchioli R, Manuzzi L, Vianello F, et al. Obstetric and delivery outcome of pregnancies achieved after laparoscopic myomectomy. Fertil Steril 2006l;86(1):159-165. Epub 2006 Jun 9.
15. Pritts EA. Fibroids and infertility: a systematic review of the evidence. Obstet Gynecol Surv 2001;56(8):483-491.
16. Hart R, Khalaf Y, Yeong CT, Seed P, Taylor A, Braude P. A prospective controlled study of the effect of intramural uterine fibroids on the outcome of assisted conception. Hum Reprod 2001;16(11):2411-2417.
17. Bingol B, Gunenc Z, Gedikbasi A, et al. Comparison of diagnostic accuracy of saline infusion sonohysterography, transvaginal sonography and hysteroscopy. J Obstet Gynaecol 2011;31(1):54-58.
18. Almog B et al., Oral presentation 260, European Society of Human Reproduction and Embryology (ESHRE), June 2009.
19. Dubuisson JB, Fauconnier A, Chapron C, Kreiker G, Nørgaard C. Reproductive outcome after laparoscopic myomectomy in infertile women. J Reprod Med 2000;45(1):23-30.